



Declaration under 37 C.F.R. §1.132

In re patent application of
Hammarström et al.
US serial No. 09/521,742
Filed: 9 March, 2000
For: Matrix Protein Compositions for Induction of Apoptosis

Assistant Commissioner for patents
Washington D.C. 20231

Sir:

I, Ståle Petter Lyngstadaas, hereby declare as follows:

- I am currently a professor at the Faculty of Odontology at University of Oslo in Norway.
- A copy of my Curriculum Vitae is attached hereto as Appendix A.
- A copy of my list of publications is attached hereto as Appendix B.
- I am one of the named inventors for the instant application.
- I have received the Official Action dated 25 March, 2003, regarding this application, and offer the following comments with respect thereto.

In developing teeth, as well as in all other developing tissues, apoptosis is today a well-known and documented phenomena, (see Yamamoto et al., J Craniofac Genet Dev Biol. 1998 Jan-Mar; 18(1): 44-50. Ultrastructural and histochemical changes and apoptosis of inner enamel epithelium in rat enamel-free area). Apoptosis has as of lately been proven to be a both necessary and beneficial process for forming the developing organism. E.g., in the late secretory and transition ameloblasts, and adjacent stratum intermedium, evidence of apoptosis of ameloblasts have been observed. When related to the occurrence of apoptosis during amelogenesis, the relative intensity of expression of Bax and Bcl-2 changes in a pattern consistent with that observed in other cell lines. (Kondo et al., Arch Oral Biol. 2001 Jun; 46(6): 557-68. The immunohistochemical localization of Bax and Bcl-2 and their relation to apoptosis during amelogenesis in developing rat molars.)

Enamel matrix proteins are proteins, which are normally present in enamel matrix, i.e. the precursor for enamel during the development of the mammalian teeth (Ten Cate: Oral Histology, 1994; Robinson: Eur. J. Oral Science, Jan. 1998, 106 Suppl. 1:282-91).

In general, such proteins have a molecular weight below 120,000 Daltons and include amelogenins, non-amelogenins, proline-rich non-amelogenins, amelins (ameloblastin, sheathlin) and tuftelins.

It is as of today not clearly proven, which of the above-mentioned proteins or cleavage products of them, comprised in the enamel matrix, actually constitute the active fraction. On the contrary, it might well be feasible to speculate that the specific activity shown by compositions comprising enamel matrix extracts is due to its complex composition of different factors with different specific activities, and that the overall effect is achieved by a

concerted combinatorial effect. This is indeed a most common effect observed in signalling cascades and in developmental connections, as shown for e.g. neurotrophic factors, or apoptotic effectors (see e.g. Opferman JT, Korsmeyer SJ, Nat Immunol., 2003 May; 4(5): 410-5. Apoptosis in the development and maintenance of the immune system, and Sieber-Blum M., Biochem Cell Biol., 1998; 76(6): 1039-50. Growth factor synergism and antagonism in early neural crest development.).

The major proteins of an enamel matrix are known as amelogenins. They constitute about 90% w/w of the matrix proteins. The remaining 10% w/w include proline-rich non-amelogenins, tuftelin, tuft proteins, serum proteins and at least one salivary protein; however, other proteins may also be present such as, e.g., amelin (ameloblastin, sheathlin), which have been identified in association with enamel matrix.

The proteins of an enamel matrix can be divided into a high molecular weight part and a low molecular weight part, and it has been found that a well-defined fraction of enamel matrix proteins possesses valuable properties with respect to treatment of periodontal defects (i.e. periodontal wounds). This fraction contains acetic acid extractable proteins generally referred to as amelogenins and constitutes the low molecular weight part of an enamel matrix (cf. EP-B-0 337 967 and EP-B-0 263 086, see also Termine et al. 1980, and Moe D, Salling E & Kirkeby S, Scandinavian Journal of Dental Research 1984, 503-507).

At present, proteins identified in the above-mentioned low molecular fraction include enamel matrix proteins such as amelogenin, amelin, tuftelin, etc. with molecular weights (as measured in vitro with SDS-PAGE) below about 60,000 Daltons. Accordingly, the active enamel substance for inducing apoptosis in a targeted neoplasm should optimally comprise a molecular weight of up to about 40,000, but no more than 60,000 Daltons.

As is clearly shown in example 2 and 3 of the above-mentioned application, we have been able to prove the apoptotic effect of a composition comprising the lower molecular weight part of an enamel matrix on a broad variety of neoplasm-derived epithelial cells.

Enamel matrix can be prepared from developing teeth as described previously (EP-B-0 337 967 and EP-B-0 263 086). The enamel matrix is scraped off and enamel matrix derivatives are prepared, e.g. by extraction with aqueous solution such as a buffer, a dilute acid or base or a water/solvent mixture, followed by size exclusion, desalting or other purification steps, optionally followed by freeze-drying. Enzymes may be deactivated by treatment with heat or solvents, in which case the derivatives may be stored in liquid form without freeze-drying.

Today, a commercial product comprising amelogenins and possibly other enamel matrix proteins is marketed as EMDOGAIN® (Biora AB). Emdogain® is produced as described above and contains 30 mg not further specified enamel matrix protein and 1 ml vehicle solution (Propylene Glycol Alginate).

The apoptotic effect of the above mentioned EMDOGAIN® gel on e.g. human oral squamous cell carcinoma-derived epithelial cells was e.g. suitably proven in (Kawase et al., J Periodontal Res. 2000 Oct; 35(5): 291-300. 2000, Cytostatic action of enamel matrix derivative (EMDOGAIN®) on human oral squamous cell carcinoma-derived SCC25 epithelial cells).

I thus strongly believe that the apoptosis-inducing effect of EMD on the neoplasm- or carcinoma-derived epithelial cells, as shown in table 1 of the

present application, is to be attributed to the genuine mixture of different active proteins in the composition of enamel matrix proteins applied. I.e. proteins comprised in the above-mentioned low molecular fraction that includes enamel matrix proteins such as amelogenin, amelin, tuftelin, etc. with molecular weights below about 60,000 Daltons. I am also clearly convinced that the effect demonstrated *in vitro* is highly indicative of the effect that a composition comprising said enamel proteins will have in the clinical situation that is envisioned in the application.

24/9-03
Date


Signature



Page 1 of 3

Curriculum Vitae

Name: Lyngstadaas, Ståle Petter
Address: Haakonsvei 5, N-1450 Nesoddtangen, Norway
Titles: BE, DDS, PhD.

Born in Oslo January 23rd 1962. Married to Anita Østhus Lyngstadaas, (Cand. pharm, PhD) in 1988. Two children; Ole Nikolai, born November 3rd 1991, and Anne Viktoria, born March 17th 1994.

Education, work and research experience: Graduated A-level in science from Ski gymnasium in 1980. Graduated from Army officers' training school June 1981. Served as 2nd lieutenant in the Norwegian Army until September 1982. Graduated as Bachelor of Engineering (BE) with main courses in bioengineering at Oslo Technical College in June 1984. Section manager at Section for Serological Analyses, Dept. of Microbiology, Central Hospital of Akershus (SiA) until June 1986. Research technician at Department for Oral Biology, Faculty of Dentistry, University of Oslo (UiO) from November 1985 until February 1991. In charge of two field missions to Northern Norway investigating the "seal invasion" in 1987, on the instructions of Dept. of Marine Zoology, Inst. of Biology, UiO. Doctor of Dental Surgery (DDS) in June 1991. Research fellow at Department for Oral Biology, the Faculty of Dentistry, UiO and the Biotechnology Centre of Oslo (BiO), from February 1991. Ph.D. thesis "On the molecular biology of tooth formation" November 1995, UiO. Visiting researcher to Prof. Irma Thesleff at the Institute of Biotechnology, University of Helsinki, Finland, in December 1995 and April to June 1996. Postdoctoral fellow at Department of Oral Pathology, Faculty of Dentistry, UiO from September 1996 until June 1997. Associate professor at Department of Pathology, Faculty of Dentistry, UiO from July 1997 to December 1999. Visiting researcher at Center for Craniofacial Molecular Biology, University of Southern California from December 1998 until February 1999. Associate professor at Clinical Research Laboratory, Faculty of Dentistry, UiO from January 2000 to April 2001. Established and managed the preclinical research laboratory and animal experiment unit at Biora AB, Malmö, Sweden, between May 1997 and February 2001 (ten employees). Professor in Biomaterial Sciences at Clinical Research Laboratory, Faculty of Dentistry, UiO since May 2001. Practicing dentistry one day a week at Årvoll tannhelse since February 1991, and from January 1993 at Majorstuen tannlegesenter AS.

Administration: Member of The Faculty of Dentistry research council, UiO 1993-1997, and from 2002 on. Member of the University Central Committee for Research and Education, UiO, 1994. Deputy chairman of Oslo Biochemistry Association, 1996, chairman in 1997. Member of organizing committee in the European Union (EU) COST B8 "odontogenesis" project 1996-2001. Vice-chairman at Dept. of Oral Pathology in 1997. Organized international workshop on the "Morphogenesis and molecular biology of enamel" in April 1998 and on "Formation and regeneration of dental tissues" in October 1999 and "The bio-implant interface" in April 2002. Member of the scientific advisory board of Biora AB, Malmö, Sweden since June 1997. Member of Clinical Research Committee (CRC) Biora AB since June 1999. Member of the Management Committee of the EU 5th framework "growth" project "Surface Improvement of Metal Implants" (SIMI) since February 2001. Coordinator and leader of the 2 year EU/Madam Curie project "Biologically induced, guided bone neogenesis started March 2001. Member of the University of Oslo board for Biotechnology, Molecular biology and Bioinformatics (EMBIO) since February 2001. Initiator, project coordinator and principal investigator in the 4 year, 2,8 million €, EU fifth framework Quality of Life project "stable extracellular matrices as novel biotherapeutics for biomimetic induction of hard tissue growth (QLK3-CT-2001-00090, Matrix)" started January 2002.

Judging committees: Administrator of the judging committee for scholarships from the University of Oslo board for Biotechnology, Molecular biology and Bioinformatics (EMBIO), fall 2001. Administrator of the judging committee for Postdoc positions from the University of Oslo board for Biotechnology, Molecular biology and Bioinformatics (EMBIO), fall 2001.

Postgraduate courses: Laboratory animal techniques, National institute of Health and Institute of Veterinary Medicine 1984. Gene technology, (BIO 351) 1987. Molecular biology (KJ-BIO 400) 1987. Forensic odontology 1990. Molecular pathology, Munich 1991. Course on "hot-lab" techniques, BiO/UiO, 1992. Nordic genome workshop, Oslo, 1994. Mouse Molecular Genetics, EMBL, Heidelberg, 1995. Ciba Symposium on Dental Enamel, London 1996. GLP and GMP practices in pharmaceutical industry, Medicin Valley Academy, Malmö 1998. Project design and control in ISO 9001, Biora AB, Malmö 2000. Intellectual Property Rights, Plougmann & Vingtoft AS and University of Copenhagen, Copenhagen 2001.

Prizes: Ciba Foundation bursar, 1996. The Zendium prize 1996. Awarded the King Harald V's gold medal for excellence in medical research 1997.

Invited lectures: NOF/IADR symposium on molecular biology, Helsinki 1991. NTF's annual meeting, Sandvika 1992. Scandinavian Association for Pediatric Dentistry, Oslo 1994. Scandinavian Association for Toxicopathology, Oslo 1995. Helsinki Biocentre lectures, Helsinki 1995. Institute of Anatomy, Faculty of Medicine, UiO, Oslo 1996. Finnish Association for Cell Biology, Helsinki 1996. Institute of Physiology, Faculty of Medicine, UiO, Oslo 1996. Institute of Cancer Research, The Norwegian Radium Hospital, Oslo 1996. Finnish Dental Association, "The Research days", Helsinki 1996. Radcliffe Hospital, University of Oxford, Oxford 1996. IX Gysinge meeting, University of Uppsala, Uppsala 1997. Opening lecture at "Karlsruhe Konferenz", Karlsruhe, 1997. Leeds University, department of Oral biology, 1998. University of Southern California, Center for Craniofacial Molecular Biology 1999. NOF/IADR symposium on molecular dentistry, Turku 1999. Seminar on Methods in Signal Transduction Investigation, Rikshospitalet, 1999. Seminar on Ribozyme Inhibition of Gene Expression, Inst. of Preclinical Sciences, Faculty of Medicine, UiO, 1999. EuroPerio Conference on Periodontal Regeneration, Oslo 1999. Futures of Swedish biotechnology industry, Stockholm Stock market May 2000. The Gordon Conference on Biomaterialization, August 2000. Pfizer meeting on hard tissue matrix biology, Sandwich, England 2001. Smith & Nephew seminar on hard tissue regeneration, York, England 2001. NTF symposium on hard tissue regeneration, Bergen 2001. Third NSCG meeting "From genes to Clinic", Turku 2002.

Editorial reviews: Acta Anatomica, Anatomical Record, Archives of Microbiology, Archives of Oral Biology, Calcified Tissues International, European journal of Oral Sciences, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Medical Genetics, Journal of Periodontology, Medical Principles and Practice, Clinical Oral Investigations, NBS-nytt, Den norske lægeforenings tidsskrift, NTF tidende.

Teaching practice: Officer and army instructor (meteorology and artillery) 1980-1982. Directed practical courses in microbiology and serology for physical chemist students at SIA in 1985 and 1986. Directed dissection course on marine mammals (BMZ 313), 1987, at Institute of Biology, UiO. Teaching biochemistry for dental students (Nucleic acids chemistry, molecular biology, cell biology and gene technology, practical courses and lectures), at The Faculty of Dentistry, University of Oslo, 1991-1996. Directed postgraduate courses in molecular biology, medical genetics and gene technology, The Faculty of Dentistry, University of Oslo, since 1992. Teaching oral pathology for dental students, lectures and practical course, 1996-2001. Teaching molecular biology in tooth formation for dental students from 1996-2002. Participating in The Dental faculty, UiO, Problem based learning (PBL) program for dental students since January 2000.

Supervising: Supervising Master- and PhD students; Christina Moinichen (DDS, 1995-1998), Eduardo Tinoco (DDS, PhD 1994-1998), Hilde Nordgarden (DDS, 1997-2003), Jacob Rønold (DDS, PhD 1999-2003), Mawan Kahdra (DDS, 2000-), Christion Skoe Bernitsen (DDS, 2002-) and Elisabeth Aurstad Riksen (DDS, 2002-) all at The Faculty of Dentistry, UiO, Heidi Berner (Cand. scient, PhD 1996-2002) at The Norwegian Radium Hospital, Anna Dackehag (Cand. Scient, MSc, 1997-1998) at Dept. of Applied Microbiology, University of Lund and Biora AB, Sweden, Caroline Paine (Cand. scient, PhD 1996-1999) at the University of Southern California, USA, and Yukio Nakamura (DDS, PhD 1999-2001) at Malmö University and Biora AB, Sweden and Showa University, Tokyo, Japan.

Research collaborations: "Ribozyme knock out of sonic hedgehog and fibroblast growth factors during tooth formation" in collaboration with Prof. Irma Thesleff, The Biocentre, University of Helsinki (1995-1997). "Inhibition of retroviral expression from pig transplants" in collaboration with Prof. Erik Larsson, Institute of Pathology, University of Uppsala (1995-1996). "The role of matrix proteins in enamel crystal formation and growth" in collaboration with Profs. Colin Robinson and Jennifer Kirkham and Dr. Steven Brookes at Dept. for Oral Biology, University of Leeds (1998-). "Matrix assembly and biomineralization" in collaboration with Prof. Malcolm Snead, Center for Craniofacial Molecular Biology, University of Southern California (1999-). "The role of enamel matrix proteins in cementum formation" in collaboration with Prof. Lars Hammarström and Dr. Ivan Slaby, Karolinska Institutet, Sweden and Dr. Axel Spahr, The Dental Faculty, University of Ulm, Germany (1998-). "Regeneration and healing in the periodontal ligament and alveolar bone" in collaboration with Dr. Stina Gestrelus, Biora AB, Sweden (1997-). "Knock out of the dentin-sialo-phosphoprotein (DSPP)" in collaboration with Dr. Helena Richie, University of Michigan (2000-2001). "Molecular templating at synthetic biomineralizing surfaces" in collaboration with prof. Samuel Snupp, University of Michigan (2001-). "The role of EdaA in submandibular gland development" in collaboration with profs. Tina Jaskoll and Malcolm Snead, University of Southern California and prof. Irma Thesleff, University of Helsinki (2001-). "cAMP response and protein kinase A activity in fibroblasts exposed to amelogenins" in collaboration with prof. Tore Jahnsen and Dr. Bjørn Skaalhegg, UiO (2000-). "The role

Page 3 of 3

of CD44 expression in enamel formation and ameloblast apoptosis" in collaboration with prof. Jahn Nesland, The Norwegian Radium Hospital (2000-). "Modelling crystal growth in maturing enamel" in collaboration with Dr. Karl I. Ugland, UiO (2001-). "Biology at the biomaterial surface" in collaboration with profs. Jan Eirik Ellingsen and Per Thrane, UiO (2001-). Participant and member of the board in the EU COST B8 "Odontogenesis" research network (1996-2001). Participant and member of the board in the EU fifth framework project "Surface Improvements of Metal Implants" (SIMI) (2001-2004). Initiator, Project Coordinator and principal investigator in the EU Industrial host, Madame Curie project "Biologically induced, guided bone neogenesis" (2001-2003). Initiator, Project Coordinator and principal investigator in the 4 year EU fifth framework Quality of Life project "stable extracellular matrices as novel biotherapeutics for biomimetic induction of hard tissue growth (Matrix)" (2002-2006).



Page 1 of 7

List of publications, Ståle Petter Lyngstadaas

Thesis:

Lyngstadaas SP. On the Molecular Biology of Tooth Formation, biomineralization; Structure, Evolution and Genetics of Calcified Dental Tissues. Dept. of Oral Biology, Faculty of Dentistry and Biothechnology Centre of Oslo, University of Oslo, Norway, November 1995.

Original articles:

Nordbø H, From SH, Iversen JA, **Lyngstadaas SP.** Organ regenerasjon – av interesse for odontologi? Nor Tannlegeforen Tid. 98:420-425 (1988)

Lyngstadaas SP, Risnes S, Nordbø H, Flønes AG. Amelogenin gene similarities in vertebrates; Amelogenin gene sequences seem to be conserved during evolution. J Comp Phys B.160:469-72 (1990)

Lyngstadaas SP. Arvemassen - en utfordring I. Nor Tannlegeforen Tid. 14:556-60 (1990)

Lyngstadaas SP, Heyden A, Nordbø H, Thrane PS. Arvemassen - en utfordring II. Nor Tannlegeforen Tid. 16:664-70 (1990)

Heyden A, **Lyngstadaas SP,** Thrane PS, Brandtzaeg P. Kan virus forårsake kreft i munnhulen? Nor Tannlegeforen Tid. 4:104-7 (1991)

Thrane PS, Heyden A, Bryne M, **Lyngstadaas SP.** Deskvamativ gingivitt - en klinisk fellesbetegnelse på flere bakenforliggende sykdommer. Nor Tannlegeforen Tid (1991)

Nordbø H, **Lyngstadaas SP.** The clinical performance of two groups of functioning class-II cast gold inlays. Acta Odontol Scand. 50:189-92 (1992)

Lyngstadaas SP, Risnes S, Sproat BS, Thrane PS, Prydz HP. A synthetic, chemically modified ribozyme eliminates amelogenin, the major translation product in developing mouse enamel *in vivo*. EMBO J. 14; 5224-5229 (1995)

Lyngstadaas SP, Crossner CJ, Nazer H, Thrane PS, Nordbø H. Severe dental berrations in familial steroid dehydrogenase deficiency; a new association. Clin. Genet. 49; 249-254 (1996)

Lyngstadaas SP, Nordbø H, Gedde-Dahl Jr. T, Thrane PS. On the genetics of hypodontia and hypoplastic teeth; Synergism or allelism of major genes in a family with six affected. J. Med. Gen. 33; 137-142 (1996)

Albandar J, Lyngstadaas SP, Forbord B. PCR primers for the amplification of the 16S rRNA gene of oral bacteria and for the specific identification of *Actinobacillus actinomycetemcomitans*. *Eur. J. Oral Sci.* 104; 144-147 (1996)

Thrane PS, Lyngstadaas SP. Ribozymes against virus diseases and cancer. *Tidsskr. Nor. Laegeforen.* 116; 1445-1446 (1996)

Mölnichen CB, Lyngstadaas SP, Risnes S. Morphological characteristics of mouse incisor enamel. *J. Anat.* 189; 325-333 (1996)

Tinoco EM, Lyngstadaas SP, Preus HR, Gjermo P. Attachment loss and serum antibody levels against *Actinobacillus actinomycetemcomitans* in localized juvenile periodontitis. *J. Clin. Periodontology* 24; 937-44 (1997)

Lyngstadaas SP, Mölnichen CB, Risnes S. Crown morphology, enamel distribution and enamel structure in mouse molars. *Anat. Rec.* ; 250: 268-280 (1998)

Lyngstadaas SP, Sproat BS, Blaschke M, Ludwig J, Rupp T, Prydz HP. In vivo knock out of a tissue specific gene by synthetic ribozymes. *Methods in Molecular Medicine. Vol 11; Therapeutic Applications of Ribozymes.* Ed: K.J. Scanlon. Humana Press Inc. Totowa, New Jersey (1998), pp 371-386

Thrane PS, Berner HS, Lyngstadaas SP. Ribozymmer – et framtidig behandlingsprinsipp ved virussykdommer og kreft. *Nor Tannlegeforen Tid.* 109:338-342 (1999)

Berner HS, Thrane PS, Lyngstadaas SP. Hvordan kan et gen gi mange forskjellige produkter? *Nor Tannlegeforen Tid* 109: 342-348 (1999)

Lyngstadaas SP, Lundberg E, Ekdahl H, Andersson C, Gestrelus S. Autocrine growth factors in human periodontal ligament cells cultured on enamel matrix derivative. *J Clin Periodontol* 28; 181-188 (2000)

Lyngstadaas SP. Nydannelse, reparasjon og regenerasjon av periodontale vev. In: *Odontologi 2000*, Munksgaard, Copenhagen; pp 167-182 (2000)

Gestrelus S, Lyngstadaas SP, Hammarström L. Emdogain – periodontal regeneration based on biomimicry. *Clin Oral Invest* 4:120-125 (2000)

Brookes SJ, Kirkham J, Lyngstadaas SP, Shore RC, Wood SR, Robinson C. Spatially related amelogenin interactions in developing rat enamel as revealed by molecular cross-linking studies. *Arch Oral Biol* 45: 937-943 (2000)

Paine CT, Paine ML, Luo W, Okamoto CT, Lyngstadaas SP, Snead ML. A Tufelin-interacting Protein (TIP39) Localizes to the Apical Secretory Pole of Mouse Ameloblasts. *J Biol Chem* 275: 22284-22292 (2000)

Lyngstadaas SP. Synthetic ribozymes as tools in gene expression. *Crit Rev Oral Biol Med.* 12: 469-78 (2001)

Nakamura Y, Hammarström L, Lundberg E, Ekdahl H, Matsumoto K, Gestrelus S, Lyngstadaas SP. Enamel matrix derivative induces reparative dentin formation. *Adv Dent Res.* (2001)

Spahr A, Lyngstadaas SP, Boeckh C, Andresson C, Ehrlich M, Podbielski A, Haller B. Effect of the enamel matrix derivative Emdogain on the growth of periodontal pathogens in vitro. *J Clin Periodontol* 29: 62-72 (2002)

Spahr A, Lyngstadaas SP, Slaby I, Haller B, Boeckh C, Tsoulfidou F, Hammarström L. Expression of Amelin and trauma induced dentin formation. *Clin Oral Investig* 6: 51-57 (2002)

Nakamura Y, Hammarström L, Matsumoto K, Lyngstadaas SP. Enamel proteins induce dentin formation in pulpotomized miniature swine permanent teeth. *J. Endodontics.* 35: 407-417 (2002)

Brookes SJ, Lyngstadaas SP, Robinson C, Shore RC, Wood SR, Kirkham J. Enamelin compartmentalization in developing porcine enamel. *Connect Tissue res* 43: 477-481 (2002)

Sculean A, Windisch P, Keglevich T, Fabi B, Lundgren E, Lyngstadaas SP. Presence of enamel matrix protein derivative on human teeth following periodontal surgery. *Clin Oral Investig* 6: 183-187 (2002)

Lyngstadaas SP, Ellingsen JE, Spahr A, Slaby I. Inducing Bone Growth Using Extracellular Matrix Proteins. In: Ellingsen and Lyngstadaas (Eds.) *The Bio-Implant Interface; Improving Biomaterials and Tissue Reactions.* CRC Press, Boca Raton. In press (2003)

Ronold HJ, Lyngstadaas SP, Ellingsen JE. A study on the effect of dual blasting with TiO₂ on titanium implant surface on functional attachment in bone. *J. Biomed. Mater. Res.* in press (2003)

Ellingsen JE, Lyngstadaas SP. Increasing biocompatibility by chemical modification of titanium surfaces. In: Ellingsen and Lyngstadaas (Eds.) *The Bio-Implant Interface; Improving Biomaterials and Tissue Reactions.* CRC Press, Boca Raton. In press (2003)

Electronic publications:

Lyngstadaas SP. Hypodontia and microdontia in an ectodermal dysplasia family with six affected members. *The London Dysmorphology Database* (1999)

Lyngstadaas SP. Dental aberrations in familial steroid dehydrogenase deficiency. *The London Dysmorphology Database* (1999)

Berner H, Lyngstadaas SP. *Schizosaccharomyces pombe* CD44 homologue genomic DNA. Genomic survey sequence. *GenBank report AF027975* (1998)

Berner H, Lyngstadaas SP. Schizosaccharomyces pombe PCR product using primers specific for human CD44 exon 9 and 16. Genomic survey sequence. GenBank report AF027976 (1998)

Berner H, Lyngstadaas SP. Hordeum vulgare CD44 homologue genomic DNA. Genomic survey sequence. GenBank report AF028348 (1999)

Berner H, Lyngstadaas SP. Strongylocentrotus droebachiensis CD44 homologue gene. Partial sequence. GenBank report AF030375 (1999)

Books

Ellingsen JE and Lyngstadaas SP (Eds.) The bio-implant interface. CRC press, Boca Raton, Florida, USA (in press)

Compendiums:

Forbord B, Lyngstadaas SP. Genteknologi for tannlegestudenter, UiO 1992

Lyngstadaas SP. Medical genetics for dentists, UiO 1996

Patents:

Lyngstadaas SP, Hammarström L, Slaby I, Andersson C, Gestrelus S, Hammargren T: Matrix protein compositions for wound healing. PCT/IB99/00337, WO9943344A (1998)

Lyngstadaas SP, Hammarström L, Slaby I, Andersson C, Gestrelus S, Hammargren T: Matrix protein compositions for wound healing. US 09/258,613 (1998)

Lyngstadaas SP, Gestrelus S, Hammarström L: Matrix protein compositions for induction of apoptosis. PCT/IB00/00245 (1999)

Lyngstadaas SP, Gestrelus S, Hammarström L: Matrix protein compositions for induction of apoptosis. US 09/521,742 (1999)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for grafting. PCT/IB00/00247 (1999)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for grafting. US 09/521,907 (1999)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for dentin regeneration. PA (PCT) 2000 01665 (2000)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for dentin regeneration. US 60/213,790 (2000)

Lyngstadaas SP, Ellingsen JE: Medical prosthetic devices and implants having improved biocompatibility. PCT/IB01/02301 (2000)

Lyngstadaas SP, Ellingsen JE: Medical prosthetic devices and implants having improved biocompatibility. US 60/254,987 (2000)

Gestrelus S, Lyngstadaas SP: Matrix protein compositions for inhibition of epithelial cell growth. PA (PCT) 2000 00968 (2000)

Gestrelus S, Lyngstadaas SP: Matrix protein compositions for inhibition of epithelial cell growth. US 60/213,381 (2000)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for guided connective tissue growth PA (PCT) 2001 00311 (2001)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for guided connective tissue growth US 60/subm (2001)

Lyngstadaas SP, Gestrelus S: Matrix protein compositions for systemic treatment. PA30325DK01 (2001)

Lyngstadaas SP, Ellingsen JE: Medical prosthetic devices and implants having improved biocompatibility. PA DK 2002 000515 (2002)

Lyngstadaas SP, Ellingsen JE: Medical prosthetic devices and implants having improved biocompatibility. PA US 10/010 140 (2002)

Published abstracts and reports:

Lyngstadaas SP, Nordbø H, Iversen JO, From SH. Methods for the study of polyphyodontism in fish. J Dent Res. 68:701 (1989)

Lyngstadaas SP, Nordbø H, Flønes AG. Nucleic acid probe search for the gene encoding amelogenin. J Dent Res. 68:938 (1989)

Lyngstadaas SP, Nordbø H, Risnes S. Phylogenetic similarities in vertebrate tooth formation. J Dent Res. 4:834 (1991)

Lyngstadaas SP, Heyden A, Høyheim B, Thrane PS, Nordbø H. Application of molecular biology in the study of tooth formation. J Dent Res 71:1084 (1992)

Lyngstadaas SP, Høyheim B, Thrane PS, Nordbø H. Restriction map of chromosomal regions containing the human amelogenin gene. J Dent Res. 72:682 (1992)

Lyngstadaas SP. Genetikk og tenner. Nor Tannlegeforen Tid. 12:474 (1992)

Heyden A, Lyngstadaas SP, Thrane PS, Brandtzaeg P. Search for human papillomavirus (HPV) in normal oral mucosa. J Dent Res. 71:1097 (1992)

Nordbø H, Lyngstadaas SP. Clinical performance of class II gold inlays. J Dent Res. 72:541 (1992)

Nordbø H, Strand GV, Lyngstadaas SP. Clinical performance of class II tunnel restorations. J Dent Res. 73:939 (1994)

Lyngstadaas SP, Risnes S, Sproat BS, Thrane PS, Prydz HP. A synthetic, chemically modified ribozyme eliminates amelogenin, the major translation product in developing mouse enamel *in vivo*. In: Heidelberg University Press (EMBL), Mouse Molecular Genetics, p.178 (1995)

Lyngstadaas SP, Risnes S, Sproat BS, Prydz HP. *In vivo* effekt av et syntetisk "hammerhead" ribozym. NBS-nytt. 19;2:3 (1995)

Lyngstadaas SP, Risnes S, Sproat BS, Thrane SP, Prydz HP. *In vivo* "knock out" of AMEL gene expression during early enamel formation. J. Dent. Res. (1995)

Albandar JM, Lyngstadaas SP. PCR primers for the specific identification of Actinobacillus actinomycetemcomitans. J. Dent Res. (1996)

Tinoco EMB, Lyngstadaas SP, Gjermo P, Preus HR. Attachment loss and serum IgG levels against *A.a.* in LJP. J. Dent. Res. (1997)

Bergem HO, Gilboe I-M, Axell T, Husby G, Lyngstadaas SP, Jensen JL. Oral antifungal factors in patients with systemic lupus erythematosus (SLE). J.Dent. Res. (1998)

Jensen JL, Messelt E, Lyngstadaas SP, Koppang H. Light and electron microscope findings in minor salivary glands from sicca patients. The Gordon Research Conference on Salivary Glands (1999)

Lyngstadaas SP, Ekdahl H, Lundberg E, Andersson C, Gestrelus S. Increased TGF-beta production in PDL cells grown on Emdogain matrix. IADR (1999)

Lyngstadaas SP. Cellular responses to enamel proteins-Implications for periodontal wound healing and regeneration. EuroPerio 3 satellite conference (1999)

Lyngstadaas SP, Andersson C, Lundberg E, Ekdahl H. Interleukin expression in cultured human PDL cells growing on Emdogain. J. Dent. Res. 79:517 (2000)

Lyngstadaas SP. Dissecting biomineralisation with ribozymes. The Gordon Research Conference on Biomineralisation (2000)

Lyngstadaas SP, Spahr A, Andersson C. Periodontal pathogenic bacterial growth inhibited by Emdogain. Medicon Valley Bio-Conference (2000)

Lyngstadaas SP, Ekdahl H, Lundberg E, Andersson C, Gestrelus S. Autocrine growth factors from PDL cells growing on enamel matrix derivative. Medicon Valley Bio-Conference (2000)

Gestrelus S, Persson E, Ölund K, Andersson C, Ekdahl H, Lundberg E, Spahr A, Bratthall GT, Lyngstadaas SP. Emdogain Gel-A ready-to-use formulation for regenerative periodontal treatment. *J. Dent. Res.* 79:576 (2000)

Rønold HJ, Ellingsen J-E, Lyngstadaas SP. Functional attachment and bone contact in microrough titanium implants. Sixth World Biomaterials Congress (2000)

Brookes S, Kirkham J, Shore RC, Wood SR, Robinson C, Lyngstadaas SP. Enamel matrix architecture revealed by molecular cross-linking of amelogenins. The Gordon Research Conference on Biomineralisation (2000)

Nakamura Y, Lundberg E, Ekdahl H, Hammarström L, Matsumoto K, Gestrelus S, Lyngstadaas SP. Enamel matrix derivative induces reparative dentin formation. Medicon valley Bio-Conference (2000)

Gestrelus S, Persson E, Ölund K, Andersson C, Ekdahl H, Lundberg E, Spahr A, Bratthall GT, Lyngstadaas SP. Emdogain Gel for regenerative periodontal treatment. Medicon Valley Bio-Conference (2000)

Nakamura Y, Lundberg E, Ekdahl H, Hammarström L, Matsumoto K, Gestrelus S, Lyngstadaas SP. Induction of dentin formation in miniature swine with enamel matrix derived proteins. International meeting on signaling mechanisms in dentin development regeneration and repair, Tessaioniki (2000)

Sculean A, Windisch P, Kevlevich T, Lyngstadaas SP. Presence of Emdogain on human teeth following periodontal surgery. *J. Dent. Res.* 80: 701 (2001)

Lyngstadaas SP, Spahr A, Andersson C. Growth of gram negative periodontal pathogenic bacteria is inhibited by Emdogain. *J. Dent. Res.* 80: 723 (2001)

Brookes SJ, Lyngstadaas SP, Shore RC, Robinson C, Wood SR, Kirkham J. Enamel-mineral and enamel-matrix protein interactions in developing porcine enamel. *IADR* (2001)

Shore RC, Bäckman B, Brookes SJ, Robinson C, Lyngstadaas SP, Kirkham J. Amelogenesis Imperfecta. British Society for Dental Research (2001)

Shore RC, Bäckman B, Brookes SJ, Robinson C, Lyngstadaas SP, Kirkham J. An SEM investigation of "pitted" and "local" hypoplastic Amelogenesis Imperfecta. *J. Dent. Res.* 80: 617 (2001)

Lyngstadaas SP. Matrix guided dento-alveolar regeneration. Third Nordic seminar on Craniofacial Growth (NSCG), Turku, Finland (2002)

Spahr A, Slaby I, Hammarström L, Lyngstadaas SP. Amelin expression during reparative dentin formation. *J. Dent. Res.* 80: 652 (2001)

Nakamura Y, Gestrelus S, Hammarström L, Matsumoto K, Lundberg E, Ekdahl H, **Lyngstadaas SP**. Enamel matrix derivative induces dentin formation. J. Dent. Res. 80: 652 (2001)

Mirastschijski U, Konrad D, Lundberg E, **Lyngstadaas SP**, Ågren M. Enamel matrix derivative: A new Wound healing agent? German Association for Wound Healing, Hamburg, Germany (2002)

Mirastschijski U, Konrad D, **Lyngstadaas SP**, Ågren M. Enamel matrix derivative stability and biological function in chronic wounds. World Conference on Wound Healing, Baltimore, USA (2002)

Rønold HJ, **Lyngstadaas SP**, Ellingsen JE. The effect of surface roughness on functional attachment measured by tensile testing. European Association for Osseointegration (2002)

Rønold HJ, Ellingsen J-E, **Lyngstadaas SP**. Bone bonding assessed by tensile testing of osseointegrating coin-shaped titanium implants. J. Dent. Res. In press (2002)

Berntsen BS, Riksen EA, Rønold HJ, Ellingsen JE, **Lyngstaaas SP**. Molecular force probing of amelogenin-titanium interactions. Third Nordic seminar on Cranofacial Growth (NSCG), Turku, Finland (2002)

Riksen EA, Berntsen BS, Rønold HJ, Ellingsen JE, **Lyngstaaas SP**. An in vivo method for measuring extracellular matrix guided osseointegration. Third Nordic seminar on Cranofacial Growth (NSCG), Turku, Finland (2002)